Original Article

ROLE OF INDOMETHACIN IN THE PASSAGE OF URETERIC CALCULI

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ABSTRACT

OBJECTIVE: To see the effectiveness of Indomethacin in the passage of ureteric calculi in our set up.

DESIGN: A descriptive study.

PLACE AND DURATION OF STUDY: This study was conducted at Department of Surgery in collaboration with Department of Pharmacology at Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan from January 1995 to December 2002.

PATIENTS AND METHODS: This study was carried out on 150 patients with radio opaque ureteric stones having transverse diameter of 3 mm to 7 mm. Patients with severe hydronephrosis, congestive cardiac failure, peptic ulcer, gastritis, hepatorenal impairment, known hypersensitivity to NSAIDs, coagulation disorders were excluded. Children under 14 years of age, pregnant and lactating mothers were also excluded.

A proforma with detail history and investigations related to renal functions was filled in every case. Intravenous infusion of indomethacin; 100 mg (2 ampules of Meglumine Indomethacinate) in 500 ml of 5% Dextrose water for a period of 2 hours once daily for 1 to 2 weeks was given to all these patients and the relief of pain and passage of ureteric calculi was monitored.

RESULTS: One hundred and fifty patients including 120 males (80%) and 30 females (20%) with male female ratio (4:1) having mean age of 28.8 years were enrolled in this study. Highest presence of ureteric calculi was seen in 21-40 years. 143 patients (95.34%) passed stones within 1-4 weeks period, 7 patients (4.66%) did not pass stones. 132 patients (88%) had complete pain relief while 18 patients (12%) had partial pain relief and needed other drugs.

CONCLUSION: NSAIDs especially indomethacin could well be tried in urinary calculi which are smaller in size before resorting to surgical measures.

KEY WORDS: ***Indomethacin. Ureteric Calculi. Management. Pakistan.***

INTRODUCTION

Ureteric Calculi are a relatively common problem and up to 80% of patients with calculi who are untreated, experience one or more recurrences within five years[1]. They are common cause of haematuria, pain in abdomen, flank and groin[2]. Ureteric Calculi originate in the kidney and due to gravity and peristalsis pass spontaneously down to the ureter[3]. Most stones with 5 mm or less in diameter pass spontaneously and a trial of conservative management is worthwhile[4].

Hypercalciuria is one of the most common metabolic derangement, and is responsible for calcium nephrolithiasis in patients[5]. Cyclo-oxygenase enzyme play an important role in the formation of Renal Prostaglandin E_2 which may participate not only in calcium stone formation by regulating the renal tubular handling of calcium, but also causes the inflammatory response which leads to edema of ureteral wall and pain by stimulation of tensoreceptors [6,7]. So the Cyclooxygenase enzyme inhibitors may produce the analgesic and anti-inflammatory action which might decrease the edema of ureteral wall and increase the peristaltic movements and may finally result in the passage of calculi through ureter[8].

Hence, the study was conducted to evaluate the effects of indomethacin in the passage of ureteric calculi in our set up.

PATIENTS AND METHODS

This study was carried out from January 1995 to December 2002 in Department of Surgery with collaboration of Department of Pharmacology at Liaquat University Hospital Jamshoro, Pakistan. One hundred and fifty patients were included in

study. All the patients with radio opaque ureteric stones with transverse diameter of 3 mm to 7 mm were included. While the patients with severe hydronephrosis requiring urgent intervention, patients with congestive cardiac failure, peptic ulcer, gastritis, hepatorenal impairment, coagulation disorders and known hypersensitivity to NSAIDs were excluded. Children under 14 years of age, pregnant and lactating mothers were also excluded from the study.

A proforma was filled in, which included details about history of ureteric colic, haematuria, burning micturition and history of passing stones. Investigations like urine analysis, blood examination, blood urea, X-ray abdomen, ultrasonography and stone analysis were carried out in all patients.

All patients received 100 mg of Indomethacin (2 ampules of meglumine Indomethacinate) in 500 ml of 5% Dextrose water for a period of 2 hours once daily for 1 – 2 weeks. The dose was repeated if the stones were not passed and this was done for a maximum of 4 weeks period. An informed consent was taken from all study participants.

RESULTS

Of 150 patients included in this study, there were 120 males (80%) and 30 (20%) females with male to female ratio of 4:1. The age ranged from 15 to 65 years with a mean of 28.8 years. Most of cases of ureteric calculi were seen in 21 to 40 years of age group. (**Table-I**). 130 patients (86.66%) presented with ureteric colic, 5(3.33%) had haematuria, 7(4.66%) had complain of backache and 8 (5.33%) were picked up incidentally (**Table-II**).

On investigations, urine analysis revealed microscopic haematuria in 110 patients (73.33%) and pus cells in 46 patients (30.66%). X-ray abdomen showed right-sided stones in 86 patients (57.33%), left sided stones in 60 (40%) and bilateral stones in 4 (2.66%). Size of stone was < 5 mm in 25 (16.66%) cases and 5-7 mm in 125 (83.33%) patients. Raised blood urea was found in 2 patients (1.33%). Sonographic findings revealed mild hydronephrosis in 90 patients (60.00%), moderate hydronephrosis in 22 patients (14.66%) and no hydronephrosis in 38 patients (25.33%). (**Table-III**)

After Indomethacin therapy, 81 patients (54%) passed stones in first week, 17 patients (11.33%) passed in second week, 14 patients (9.33%) in third week, 31 patients (26.66%) in fourth week and 7 patients (4.66%) did not pass the stone even after four weeks of therapy. (**Table-IV**) Stone analysis revealed calcium oxalate in 110 patients (73.33%), phosphate stones in 22 patients (14.66%) and mixed stones in 11 patients (7.33%). (**Table-V**)

TABLE I
SHOWING AGE AND SEX DISTRIBUTION OF CASES

Age Group	Males	Females
15-20 years	10(6.66%)	02(1.33%)
21-30 years	40(26.66%)	08(5.33%)
31-40 years	50(33.33%)	14(9.33%)
41-50 years	15(10%)	06(4%)
51-65 years	05(3.33%)	0(0%)
Total	120(80%)	30(20%)

TABLE II
SHOWING CLINICAL FEATURES OF CASES

Symptoms	No. of Patients	%
Ureteric Colic	130	86.66%
Haematuria	5	3.33%
Backache	7	4.66%
Unrelated symptoms	8	5.33%
Total	150	100%

TABLE III
SHOWING FINDINGS OF DIFFERENT INVESTIGATIONS

Investigations	No. of Patients	%
1. Urine Analysis:		
Microscopic Haematuria	110	73.33%
Pus Cells	40	26.67%
Total	150	100%
2. X-Ray Abdomen:		
Right Sided Stones	86	57.33%
Left Sided Stones	60	40%
Bilateral Stones	4	2.66%
Total	150	100%
3. Size of stone on X-Ray:		
< 5 mm	25	16.66%
5 - 7 mm	125	83.33%
3. Raised blood Urea	02	1.33%
4. Sono-graphic Findings:		
Mild Hydronephrosis	90	60%
Moderate Hydronephrosis	22	14.66%
No Hydronephrosis	38	25.33%
Total	150	100%

TABLE IV
SHOWING TIME DURATION OF PASSAGE OF STONE AFTER INDOMETHACIN THERAPY

No. Of patients	Time Duration	(%)
81	First week	54.00%
17	Second week	11.33%
14	Third week	9.33%
31	Fourth week	20.68 %
07	Not passed stone even after Four weeks	4.66%
Total = 150		100%

TABLE NO. 5
SHOWING STONE ANALYSIS

No. Of patients	Time Duration	(%)
110	Calcium oxalate	73.33%
22	Phosphate	14.66%
11	Mixed	7.33%
07	Did not pass stone	06%
Total = 150		100%

DISCUSSION

The use of Indomethacin is a non-conventional method of treating urinary calculi. Stone size and location are to be considered when evaluating the possibility of passage[9].

In the presence of ureteric stones, the Prostaglandin E_2 is responsible for increase in Glomerular filtration rate and induces diuresis by opposing the action of anti diuretic hormones on the renal tubule, thus the intrapelvic pressure is increased and impaction of the stone leads to further pain and inflammation[10]. Indomethacin acts by various mechanisms; it has analgesic and anti inflammatory property by inhibition of prostaglandin E_2 synthesis. The other mechanism of Indomethacin has been found to decrease calcium excretion in hypercalciuric and normocalciuric groups. The advantage is that it does not alter the creatinine clearance and thus maintains the kidney function[6].

Urinary calculi are very common problem and 50% of patients present between the ages of 30 to 50 years[11]. However, in our study maximum incidence was seen in between 21 to 40 years of age (59.99%). Male to female ratio is variable in different studies. Male to female ratio given by Francis X etal in their study was 3:1[12]. But in our study, male to female ratio is 4:1.

Patients with ureteric stones classically present with severe unilateral colicky abdominal pain which can radiate to groin subsequently in scrotum or labia depending upon the site of stone. Also nausea and vomiting are common features[4] in our study. Majority of patients presented with the symptoms of ureteric colic (86.66%) and only few patients presented with haematuria (3.33%) and backache (4.66%).

A study have been conducted by Al waili NS, in which Indomethacin suppositories were used and patients passed stones within 30 days. Stones less than 3 mm in diameter in lower ureter were passed spontaneously in 90% of cases and those more than 3 mm in size and in upper ureter were not passed in most cases[13].

In our study, 95.34% patients passed stones in one month and 4.66% did not pass stones at all and needed surgical intervention. Complete pain relief was the primary aim and was achieved in 88% of the cases.

Commonest stones found in Great Britain are calcium oxalate 39.4%, calcium phosphate 13.2%, mixed calcium oxalate and phosphate 20.2%, struvite 15.4%, uric acid 8% and cystine 2.8%[14]. In our study, calcium oxalate stones were present in 73.33%, phosphate stones in 14.66% and mixed stones in 7.33% of patients. Indomethacin by inhibiting cyclooxygenase enzyme inhibits calcium oxalate up take by renal cells and hence decreases the formation of urinary calculi[15].

So, the Indomethacin not only increases the passage of ureteric calculi but also decrease its formation.

CONCLUSION

Non-steroidal anti-inflammatory drugs could well be tried in conservative management of urinary calculi including their passage per urethera before surgical measures and pain relief without opiates and anti spasmodics.

Intravenous infusion of Indomethacin should be employed after evaluating the size and site of stone and possibility of its passage.

Prevention is the corner stone in the management of recurrence; high intake of water and analysis of stones may identify specific preventive measures.

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